The Effects of Various Metal Ions on the Folding of G-Quadruplexes

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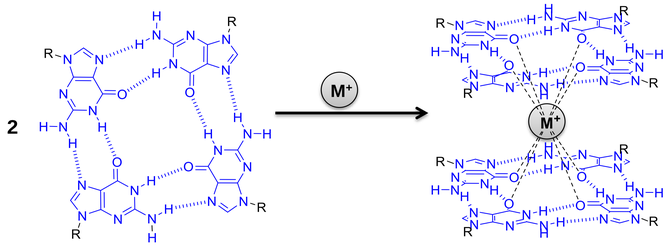
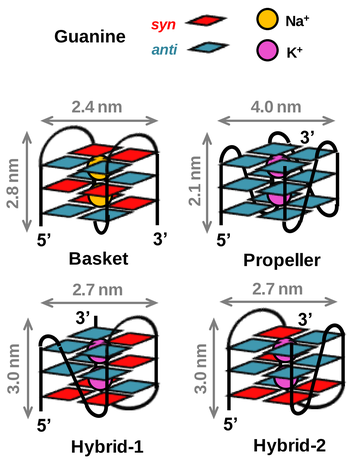
Introduction



G-quadruplexes are nucleic acid sequences that are rich in guanine and are capable of forming a four stranded structure. Four guanine bases can associate through hydrogen bonding to form a square planar structure called a guanine tetrad, and two or more guanine tetrads can stack on top of one another to a form a G-quadruplex. Depending on the direction of the strands or parts of a strand that compose the tetrad, structures may be described as parallel or anti-parallel leading to various folds.



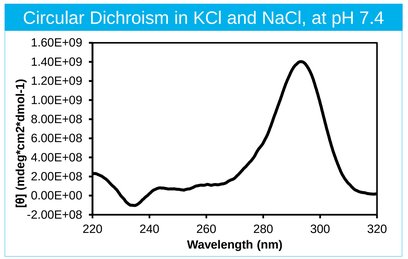
The telomere ends of chromosomes are composed of tandem repeats of a G-rich sequence 5'-$(TTAGGG)_n$-3' that can fold into various G-quadruplexes, including the hybrid, basket, and propeller folds under different physical conditions. These conditions include the presence of metal ions such as potassium or sodium. Mutations and other physiological factors can influence the G-quadruplex folds.

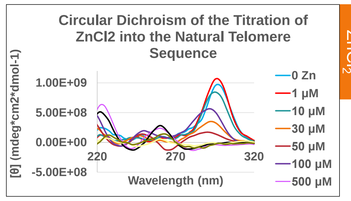
Abstract

The objective of the following research is to determine how various metal ions interact with specific DNA sequences in order to alter the formation, i.e. the folding, of G-quadruplexes. The characteristic property of a G-quadruplex structure is stabilization brought on by the presence of metal cations that sit in the central channel between the tetrads. Differentiation in metal cations have been shown to alter the stability and folding topology of G-quadruplex sequences.

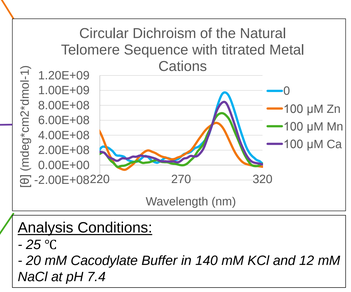
Natural Telomere

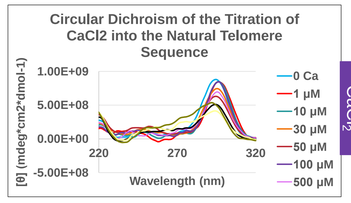
5`-GGGTTAGGGTTAGGGTTAGGG-3`



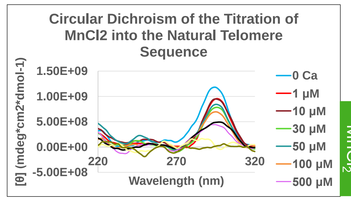


$ZnCl_2$





$CaCl_2$

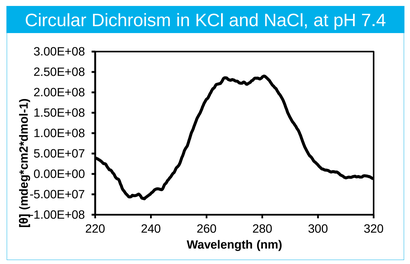


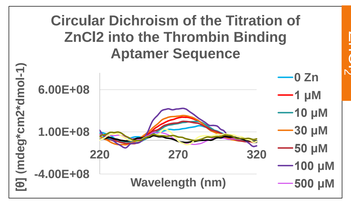
$MnCl_2$

Analysis Conditions:
- *25 ℃*
- *20 mM Cacodylate Buffer in 140 mM KCl and 12 mM NaCl at pH 7.4*

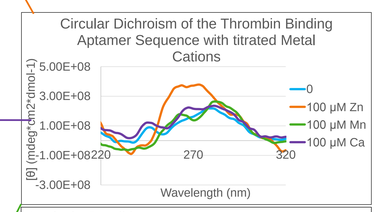
Thrombin Binding Aptamer

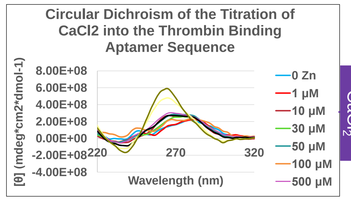
5`-GGTGGTGTGGTGG-3`



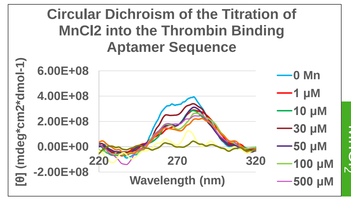


$ZnCl_2$





$CaCl_2$



$MnCl_2$

Analysis Conditions:
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Conclusion

Under oxidative stress, divalent cations are released from the proteins they are bound to give cellular concentrations of 100 μM Zn^{2+} , 1-10 μM Ca^{2+}, and 1-10 μM Mn^{2+}. On the basis of the titration CD studies, as the divalent cations concentrations increased they were found to inhibit the folding of the G-quadruplex structures. The ability for divalent metals to coordinate with the phosphate groups and the heteroatoms of the guanine heterocycle in the G-quadruplex leads to the inability to maintain strong coordination with K^+ in the interior of the channel and loss of the structure. Curiously, $ZnCl_2$ at 500 μM began to produce a mirrored G-quadruplex CD spectrum that is not commonly observed. The initial interpretation of this mirrored result suggests a reordering of the G-quadruplex structure to the opposite helical twist. Future studies will explore this hypothesis. Additional future work will conduct studies outside the realm of biologically relevant concentrations in order to determine if there exist any unique structural and physical properties these structures can adopt. New structural motifs may find scientific relevance in DNA materials, for example

Works Cited

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